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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,401	09/11/2008	C. Frank Bennett	ISPH-0852USA	5614

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
07/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/559,401	BENNETT ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,26-30,33-42,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24, 26-30, 33-42, 44, 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 5-17-10.

Claims 24, 26-30, 33-42, 44, 45 are pending in the instant application.

Response to Arguments and Amendments

Withdrawn Rejections

Applicant's arguments with respect to claims 24-43 have been considered but are moot in view of the new ground(s) of rejection set forth below.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al (WO 92/03139) and Bennett et al (USPN (USPN 6,077,833), the combination in view of Wright et al (USPN 5,795,876), Cook et al (USPN 6,440,943) and Wollyniec et al (Am. J. Resp. Cell & Molec. Biol., Vol. 18, pages 777-785, 1998), the combination further in view of Wang et al (USPN 6,403,566).

The claims are drawn to methods of reducing eosinophilia recruitment into the lung in a human comprising administration of an antisense oligonucleotide of SEQ ID NO. 22, or of an antisense which comprises 8-50 nucleobases and comprises SEQ ID NO. 22, which specifically targets and inhibits the expression of ICAM-1 of SEQ ID NO. 138, and which optionally comprises 2'-O-methoxyethyl modified sugars, phosphorothioate internucleotide linkages, 5-methyl cytosines, bicyclic sugars, and which optionally comprises 5' wing – gap - 3' wing segments, and which antisense inhibits the expression of ICAM 1 and which is optionally co-administered with a steroidal anti-inflammatory agent

Bennett et al (WO 92/03139) teach the antisense oligonucleotide of SEQ ID NO. 22, and antisense which comprise 8-50 nucleobases and comprise SEQ ID NO. 22, which specifically targets and inhibits the expression of ICAM-1 of SEQ ID NO. 138 in humans, and which optionally comprises 2'-O-methoxy modified sugars, phosphorothioate internucleotide linkages (See the entire document, esp. SEQ ID NO. AAQ22650 and the claims).

Bennett et al (USPN 6,077,833) teach the antisense oligonucleotide of SEQ ID NO. 22, and antisense which comprise 8-50 nucleobases and comprise SEQ ID NO. 22, which specifically targets and inhibits the expression of ICAM-1 of SEQ ID NO. 138 in humans, and which optionally comprises 2'-O-methoxyethyl modified sugars, phosphorothioate internucleotide linkages, 5-methyl cytosines, and which optionally comprises 5' wing – gap - 3' wing segments, and which antisense inhibits the expression of ICAM 1, and is optionally co-administered with a steroidal anti-inflammatory agent (see entire document, esp. SEQ ID NO. 17, Fig. 6, paragraphs 14, 24, table 3, 102-106, claims 1-46, esp. claims 14-17, 41 and 43).

Bennett et al and Bennett et al do not teach antisense oligonucleotides comprising modified, bicyclic sugars, nor do they teach an in vitro assay for measuring eosinophil infiltration, nor the administration of therapeutic agents to inhibit eosinophil infiltration in the lungs.

Wright et al (USPN 5,795,876) teach the administration of antisense in vivo to inhibit eosinophil infiltration and accumulation in the lungs (see esp. paragraphs 173-175, example 19).

Cook et al (USPN 6,440,943) teach the design, synthesis, and use of antisense oligonucleotides for targeting ICAM-1, and therapeutic approaches to treating inflammatory diseases and disorders using these antisense, as well as teaching in vitro assays for eosinophil infiltration (see entire document, esp. paragraph 72).

Wollyniec et al (Am. J. Resp. Cell & Molec. Biol., Vol. 18, pages 777-785, 1998) teach reduced inflammation and eosinophilia in ICAM-1 deficient mice (see entire

document, esp. the abstract, introduction on pp. 777-8; p. 780, including Fig. 2; p. 783, including Fig. 6).

Wang et al (USPN 6,403,566) teach the design, synthesis and advantages of incorporating bicyclic sugar modifications into antisense oligonucleotides (see entire text, esp. paragraphs 1-12).

It would have been obvious to utilize the well known antisense oligonucleotide of, and comprising SEQ ID NO. 22 to target ICAM-1, of SEQ ID NO. 138, and inhibit its expression because this inhibition of ICAM1 expression using antisense, including SEQ ID NO. 22, has been shown by many in the art, including Bennett and Bennett. One would have been motivated to use antisense oligonucleotides to inhibit ICAM1 expression to treat eosinophilia because ICAM-1's involvement in inflammation and eosinophilia was well known in the art, as taught previously by Wright, Bennett, Bennett, Cook and Wollyniec. One would have been motivated to combine well known inflammation inhibitors, including steroidal agents, with the antisense to provide treatment effects for inflammation because such combination therapy had been taught previously in the art, as shown by Bennett.

One would also have been motivated to incorporate the many well known modifications, including phosphorothioate internucleotide linkages, 5-methyl cytosines, gapmers, 2'-O- sugar and bicyclic sugar modifications into antisense oligonucleotides because the technology to incorporate these modifications into antisense oligonucleotides was routine in the art at the time of the instant invention, had been taught previously by many in the art, and were well known to impart advantageous

properties to antisense, including imparting enhanced stability, target binding and cellular uptake. One of skill in the art would have reasonably expected that SEQ ID NO. 22, and including the modifications claimed, would provide for inhibition of ICAM1 expression in vitro and in vivo, and would provide for the treatment effects claimed, including reducing inflammation and reducing eosinophilia, relying on the prior art teachings of Wright, Bennett, Bennett, Cook, Wang and Wollyniec.

For these reasons, the instant invention would have been obvious to one of ordinary skill in the art at the time of filing.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** The examiner's office hours are generally Monday-Friday, 10:30am - 7pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris

Low, can be reached on (571) 272-0951. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
7-20-10

/Jane Zara/

Primary Examiner, Art Unit 1635